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Influence of pro- and anti-inflammatory cytokines in Th1 polarization after allogeneic stimulation

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The exogenous cytokine milieu can influence Th1/Th2 polarization. Besides the differential functional properties, T lymphocytes also acquire distinct profiles of chemokine receptors. Human Th1 lymphocytes preferentially express CCR5 and CXCR3 while Th2 lymphocytes express CCR3, CCR4 and CCR8. After their polarization into Th1 cells, grafted T lymphocytes mediate the development of graft-vs-host-disease, the major complication after bone marrow transplantation. We performed mixed lymphocyte cultures for ten days, with and without addition of IL-2, IL-4, IL-10, IL-12 and IL-18 at the third and sixth day of cultures. The expression of CXCR3 and CCR5, in CD4+ and CD8+ T lymphocytes was evaluated by flow cytometry, before and after ten days of culture. The exogenous addition of IL-2 or IL-12 favoured the Th1/Tc1 phenotype and IL-4 was also capable of inducing Th1 polarization. In opposition to IL-12, IL-18 didn't induce a significant polarization into Th1 phenotype, an effect more similar to that induced by IL-10. This action could explain, at least in part, its possible protective effect in the incidence of acute and chronic graft-versus-host disease after allogeneic stem cell transplantation.

Key Words: Flow cytometry; CCR5; Th1/Th2 polarization; GVHD; IL-18